Inhibition of vascular endothelial cell growth factor activity by an endogenously encoded soluble receptor.

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Abstract

Vascular endothelial cell growth factor, a mitogen selective for vascular endothelial cells in vitro that promotes angiogenesis in vivo, functions through distinct membrane-spanning tyrosine kinase receptors. The cDNA encoding a soluble truncated form of one such receptor, fms-like tyrosine kinase receptor, has been cloned from a human vascular endothelial cell library. The mRNA coding region distinctive to this cDNA has been confirmed to be present in vascular endothelial cells. Soluble fms-like tyrosine kinase receptor mRNA, generated by alternative splicing of the same pre-mRNA used to produce the full-length membrane-spanning receptor, encodes the six N-terminal immunoglobulin-like extracellular ligand-binding domains but does not encode the last such domain, transmembrane-spanning region, and intracellular tyrosine kinase domains. The recombinant soluble human receptor binds vascular endothelial cell growth factor with high affinity and inhibits its mitogenic activity for vascular endothelial cells; thus this soluble receptor could act as an efficient specific antagonist of vascular endothelial cell growth factor in vivo.

MeSH

Alternative Splicing; Base Sequence; Cloning, Molecular; Cross-Linking Reagents; DNA Primers; DNA, Complementary; Endothelial Growth Factors; Endothelium, Vascular; Gene Expression; Human; In Vitro; Kinetics; Lymphokines; Mitogens; Molecular Sequence Data; Polymerase Chain Reaction; RNA, Messenger; Receptor Protein-Tyrosine Kinases; Receptors, Growth Factor; Solubility

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